Evidence from a variety of experimental models, coupled with intriguing clinical data, has intensified interest in using an “open lung” strategy for ventilatory management of acute respiratory distress syndrome (ARDS). In this approach, emphasis is placed on establishing and maintaining patency of potentially recruitable airspaces throughout the tidal cycle. Because positive end-expiratory pressure (PEEP) counterbalances the tendency for airway closure and small tidal volumes limit peak tidal pressure, a high PEEP/low tidal volume strategy may offer the best chance of avoiding injurious cycles of ventilation. It must be understood that PEEP holds open unstable lung units but does not itself open them. Recruitment maneuvers are intended to establish alveolar patency that may be maintained at lower tidal pressures and PEEP levels than would otherwise be required. As we investigate the role of recruitment maneuvers in the laboratory and clinic, many questions remain. Should recruitment be our objective when closed lung regions require such high pressures such that opening and closure would not otherwise occur? What is the most effective recruitment method? How should recruitment be monitored? Are serial maneuvers needed, and if so, how should they be spaced? Definitive answers will require additional laboratory and bedside investigation.

Key Words: acute respiratory distress syndrome, recruitment maneuver, positive end expiratory pressure, pressure volume loop

Fueled by overwhelming laboratory evidence and by recent results from clinical trials, injury caused by mechanical ventilation in the acute respiratory distress syndrome (ARDS) [ventilator-induced lung injury (VILI)] has become a subject of significant concern. Overdistention occurring at the end of inspiration related to excessive transalveolar pressure and the repetitive opening and closing of lung units that fail to maintain patency at end expiration are likely contributors to VILI. Simultaneous avoidance of excessive pressure and alveolar collapse is made especially challenging in ARDS because of unevenly distributed pathology and regional mechanics. To meet these objectives, many investigators now recommend keeping plateau pressure below 30 to 35 cm of water while using sufficient positive end-expiratory pressure (PEEP) to keep the lung open.

Several trials comparing low (6 to 8 mL/kg) versus conventional (10 to 12 mL/kg) tidal volumes for a given PEEP level (set empirically) failed to demonstrate the benefit of a volume limiting strategy with regard to morbidity and mortality. In contrast, 2 other studies showed a significant mortality benefit by reducing tidal volume. One of these studies combined reduction in tidal volume with use of a comparatively high PEEP level, whereas the largest controlled trial to date focused on the tidal volume question by using an identical protocol-driven strategy for PEEP in both groups. In addition, a recent clinical trial demonstrated that using high PEEP in conjunction with low tidal volume reduced concentrations of inflammatory cytokines both in the bronchoalveolar lavage fluid and in the blood. A higher PEEP level could be particularly important in a low tidal volume ventilation strategy because hypoventilation itself may lead to progressive derecruitment. Recruitment maneuvers also help to reverse atelectasis consequent to reduced tidal volume ventilation.

Lung Collapse in ARDS

Tissue elastic recoil forces and increased surface tension tend to reduce alveolar dimensions. At functional residual capacity, these forces of contraction are normally offset by the expanding force of the outwardly directed chest wall recoil and by the surface tension reducing effect of surfactant. In the setting of ARDS, however, tissue elastic recoil is increased by cellular infiltration and by loss of functioning lung units, particularly in the fibroproliferative stages of this condition. Surface tension also rises, as the alveolar lining cells that produce surfactant are destroyed and changes within the alveolar microenvironment, including exuded protein and inflammatory mediators, compromise surfactant function.

For the same alveolar pressure (approximated as the end-inspiratory “plateau”), variations of regional anatomy...
cause a spectrum of transalveolar forces and inflation conditions. In the lower lung zones, the tendency for lung unit closure is increased by a stiffer chest wall, by higher abdominal pressure, and by the superimposed weight of overlying edematous lung. In addition, the heart, which is cradled by the lower lobes of the lung in the supine position, accentuates airway collapse in dependent lung regions. To counterbalance purely hydrostatic forces and avert small airway closure, only modest airway pressures are required. If, however, gas is absorbed from the alveoli, adhesive “sticky” atelectasis develops that requires higher pressures to open.

**The Dilemma Posed by the Mechanically Heterogenous Lung**

Because of regional differences in transalveolar pressure, the nondependent alveoli of the acutely injured lung may remain fully open or be overdistended by pressures that are insufficient to reverse atelectasis in more dependent zones. Repeated application of high pressure to lung units that are collapsed gives rise to airway, as well as alveolar, damage. Delicate terminal bronchioles, unsupported by cartilage, may be subjected to luminal pressures similar to those seen in bronchi many generations proximal if they connect to nonexpandable air sacs. This exposure and susceptibility may explain the prevalence of airway disruption and pseudocysts in acutely injured lungs ventilated with high pressure. These forces also encourage permeability edema and more obvious forms of barotrauma, including pneumothorax, hemorrhage, and gas embolism.

**Importance of Lung Recruitment**

To fully understand the importance of recruitment in avoiding additional lung injury and promoting healing, it must be understood that tissue stresses at the boundaries of collapsed and open lung units are considerably greater than those in the free wall of the open alveoli subjected to the same luminal pressure. In a paper published in 1970, Mead and colleagues suggested that forces opposing lung collapse are amplified in nonlinear proportion to the magnitude of the pressure that exists in surrounding air-filled alveoli. These authors used a highly simplified geometrical argument to suggest that when alveolar pressure is at 30 cm H₂O, interfascial tension could be 4.5-fold greater at boundaries of open and closed lung units. These extreme forces, which are applied cyclically 20,000 to 40,000 times per day in the ventilation of patients with acute lung injury, could serve as one signal for formation and release of biologically active mediators of inflammation, as has been reported in a variety of experimental models. In fact, an intense neutrophilic response occurs within hours if subjecting a healthy lung to a sufficient mechanical stretching stimulus (ventilation with high pressures and low levels of PEEP). Because the lungs must accommodate the entire cardiac output, inflammatory mediators generated there have the potential to reach the systemic circulation, perhaps in quantities sufficient to produce distant organ dysfunction or injury. Experimental and clinical observations indicate that inflammatory mediators, bacteria, and gas translocate from the lung to the systemic circulation under the influence of high inflation pressures used in combination with low levels of end-expiratory pressure.

Apart from any role in inciting or up-regulating inflammation, the magnitude of these mechanical stresses is sufficient to disrupt epithelial and endothelial integrity at the gas-blood interface. Tidal opening and closure denudes epithelium at the level of the terminal bronchioles. Recent work from our laboratory indicates that the endothelial barrier may also be at risk. Hemorrhage occurs preferentially in the dependent lung regions most subject to tidal opening and closure. In addition, increasing microvascular pressure proximal to the alveolus dramatically accentuates the tendency for a given pattern of ventilation to cause damage. Computed tomography appears to confirm that application of PEEP reduces the tendency for tidal recruitment by reduction of lung collapse between breaths.

**Achieving Recruitment**

In the clinical setting of ARDS, a major challenge is to apply sufficient pressure to keep the lung fully recruited without either unduly increasing the stress applied to the tissue that remains closed or overdistending alveoli that remain fully open throughout the tidal cycle. A number of techniques have been used to accomplish this difficult objective. All methods consider that to some extent recruitment depends not only on the transpulmonary pressure applied to the airway but also on the duration of its application. Because of viscoelastance and other time dependent, force distributing phenomena, the tendency of an airway to open or “yield” is a function of transmural pressure and time. It is commonly observed that a stepped rise in end-expiratory pressure does not reinflate all collapsed alveoli simultaneously; the full volume increment is not realized for multiple tidal cycles afterward. Another important principle of lung recruitment is that the pressures required to reopen an alveolus are considerably higher than those required to keep it from closing again. This disparity accounts for the hysteresis of the static pressure-volume loop. Such observations have resulted in attempts to apply maneuvers intermittently that accomplish lung opening without subjecting tissue to potentially damaging forces that would result from the repeated application of high pressure during tidal ventilation. Recruitment maneuvers are particularly important when low-end inspiratory pressures are used, such as during high-frequency ventilation. Sighs, sustained application of high pressure in single or multiple episodes, progressive PEEP with a fixed upper limit for end-inspiratory pressure and declining tidal...
volume, and use of increased PEEP with preserved tidal volumes for brief periods with body repositioning are examples of recruitment techniques.²⁶

**Prone Positioning as an Aid to Recruitment**

Prone positioning, which has experienced resurgent popularity for treating patients with ARDS, can be considered a form of recruitment maneuver. As the weight of the heart is removed from the dependent portions of the lungs and the pleural pressure gradient redistributes, transalveolar forces increase in the dorsal zones of the lung. These enhanced forces are also sustained, helping to maintain airway patency and support alveoli opened by the increase in local transalveolar pressure.¹¹ Although proning is still not routine in medical practice, it is important to understand that the prone position is assumed naturally by many persons during sleep; as often, in fact, as the supine position in which acutely ill patients are traditionally managed for extended periods of time. It is also worth noting that all quadrupedal mammals (including our primate relatives) spend most of their time in the prone position, with the exception of those who protect themselves from enemies by suspending from tree branches (sloths and opossums) or ceilings of caves (bats).

When high inflation pressures are applied to supine experimental animals, lung damage predominates in the dependent areas subjected to highest compressive forces, as well as the highest hydrostatic vascular pressures.¹⁵ In the prone position, transalveolar forces are more evenly distributed, and hydrostatic pressure is reduced in the dorsal regions, which continue to receive the majority of blood flow. Perhaps for these reasons, ventilator-induced lung damage is less intense and its distribution less heterogeneous in the prone position.

**Potential Benefit of Spontaneous Efforts**

As pointed out many years ago, the tidal swings of pressure that ventilate the lung during spontaneous breathing are greatest in dependent regions.²⁷ As opposed to positive pressure ventilation of a passive individual, the dependent peridiaphragmatic regions tend to experience the greatest tidal excursion. This movement may be beneficial if such excursions aid in achieving the yield pressure needed for airway opening or in maintaining ventilation of marginally ventilated areas that would otherwise undergo collapse. It has been recently reported that spontaneous respiratory efforts improve gas exchange during bilevel ventilation in patients with acute lung injury, at least for some PEEP–tidal volume combinations.²⁸ Another intriguing aspect of spontaneous breathing is cycle-to-cycle variation of amplitude. A biologically variable ventilatory pattern applied by a programmed mechanical ventilator has been reported to achieve better oxygenation in the setting of experimental lung injury or postoperative atelectasis than does a uniform pattern of unchanging tidal volume associated with the same average tidal volume and minute ventilation.²⁹

**High Versus Low Tidal Volumes**

Raising tidal volume may have both beneficial and detrimental effects on VILI, depending on the tradeoff between the potentially damaging influence of higher end tidal pressure and any improved recruitment resulting from that increased stress. Other variations in tidal breathing patterns have been used to encourage sustained recruitment. Intermittent sighs that mimic the pattern observed during health have been reported to be associated with higher end-expiratory lung volume and better arterial oxygenation, particularly in patients with extrapulmonary (“secondary”) initiators of ARDS.²⁵ Frequent sighs and PEEP increases may be needed to sustain benefit, however, calling into question the wisdom of their use. Periodic applications of higher levels of end-expiratory pressure have also been reported as successful in reversing atelectasis.

**Do Pressure Volume Curves Guide PEEP Selection (Fig. 1)**

Since the earliest days of characterizing inspiratory pressure-volume relationships in isolated lungs and for the intact respiratory system, it has been clear that pressures approaching or exceeding those that accomplish total lung capacity in a normal subject are necessary to fully reverse established atelectasis. Recent experimental observations demonstrate that the inspiratory limb of the pressure volume relationship is shaped in part or in its entirety by contributions of lung units that open or overdistant at different pressures. The lower inflection zone of the inspiratory pressure volume curve, which has been widely used to guide selection of end-expiratory pressure, in fact, merely identifies the span of airway pressures over which lung unit opening begins to approach its highest incidence.³⁰ Recruitment of the stickiest and most dependent lung units may not occur until pressures exceed those corresponding to total lung capacity (TLC) within a previously “opened” lung. The upper deflection zone results not only from overdistantion, but also from progressively diminishing recruitment.³¹,³² The inspiratory contours are affected by the end-expiratory pressure from which the curve is inscribed. As pressure is gradually released from total lung capacity, those lung units most recently recruited stay inflated at pressures considerably lower than those required to open them. If the objective is to keep as many lung units open as possible, it seems likely that PEEP is best selected after such a recruitment maneuver is performed and before opened units can recollapse (Fig 2). Unfortunately, controversies regarding the nature of the recruitment maneuver, the number of recruitment maneuvers to be performed, and the method by which to monitor recruitment and the safety of recruitment efforts have prevented consensus from...
being formed regarding the merit of performing recruitment maneuvers in the clinical setting.

Lungs injured in different ways respond with varying success to recruitment maneuvers. Traditional models of lung injury (oleic acid or surfactant depletion) are more recruitable than are models in which the damage results from pneumonia or pure VILI itself. In recently published studies, for example, experimental oleic acid injury resulted in a lung that was approximately 55% recruitable, whereas primarily pneumonia-induced human ARDS was associated with less than 8% total potential recruitment. In the clinical setting, diffuse and patchy patterns of infiltration on computed tomographic (CT) scan are associated with greater tendency to respond to recruitment maneuver than are those with segmental or lobar distributions. Response to recruitment maneuvers also depends on the levels of PEEP and tidal volume in use prior to attempted recruitment. If recruitment maneuvers begin from a low level of end-expiratory pressure and a low tidal volume, the response to a recruitment maneuver is more dramatic than if recruitment maneuvers are layered onto a high tidal volume/high PEEP precondition. While the degree of success for a recruitment maneuver may be predicted from conditions prior to recruitment, setting PEEP after the intervention is essential to sustain improvement in oxygenation. Oxygenation is the critical clinical end point to which recruitment is directed. Benefits resulting from recruitment maneuvers may be either more or less obvious after a change in body position, depending on whether the position change itself recruited the great majority of collapsed and recruitable lung units or whether the position inversion added a crucial degree of stretching force to lung units that are usually refractory to opening or predisposed to closure. How Do We Assess Recruitment?

Contours of the inspiratory pressure volume curve may reflect the progress of gas exchange unit opening. When volume is expressed as a percentage of total lung capacity above functional residual capacity (FRC) and completeness of recruitment is also expressed in percentage terms, the inspired contours of volume or recruitment versus airway pressure relationships appear very similar when inflation begins from zero PEEP functional residual capacity. Because of hysteresis, however, it should be clear that the inspiratory pressure volume curve cannot reliably identify the end-expiratory level of pressure associated with sustained opening. Although expiratory decremental PEEP compliance curves

FIGURE 1. Relationship between pulmonary compliance and lung recruitment. Observe that the best compliance was obtained at PEEP levels close to P_{box} as long as low P-V are used in compliance calculations (approximately 4–6 mL/kg). Nevertheless, this coincidence is empirical, and the concordance is not always precise. Compliance values are the combined result of recruitment (increasing the compliance values) and overdistention (decreasing the compliance values). Full recruitment was only obtained at PEEP levels of 30.5 cm H_{2}O, but overdistention of many units at these high pressures depressed overall tidal compliance.

FIGURE 2. Effects of a recruiting maneuver and sustaining end-expiratory pressure on lung volume and recruitment. Stepwise definition of the P-V curve by the supersyringe technique does not achieve full recruitment, as the expiratory limb defined after a sustained recruiting maneuver or after applying a high level of PEEP (30.5 cm H_{2}O) is displaced upward along the absolute (total) volume axis (oleic acid-ALI in dog). Although not tested in this experiment, sustained application of sufficient PEEP might also succeed in approaching the expiratory "maximal envelope."
may provide additional guidance, there is currently little experimental or clinical evidence to confirm or refute their practical utility.

In a general sense, reductions in venous admixture should correlate with the opening of unstable lung units when FiO₂ is held constant. Thus, oxygenation may also be used to monitor recruitment, but the relationship is inexact. Blood gas analysis can be conducted in “real time” using indwelling arterial sensors. As arterial oxygenation should prove quickly responsive to shunt reversal, this technology holds promise for use as a bedside tool. By monitoring PaO₂, this technique represents an advance over standard saturation monitors because of greater signal amplitude and independence from the effects of pH, perfusion in skin pigmentation. Because current in-line blood gas analyzers have time-delayed response characteristics and because time is required for blood flow redistribution and hemodynamic re-equilibration following the recruitment maneuver, assessment of effect should be delayed for several minutes after such interventions. Hypoxic pulmonary vasoconstriction is one variable that may alter the distribution of blood flow and complicate utilization of oxygenation to track effectiveness of recruitment strategies. Bedside imaging techniques such as electrical impedance tomography may ultimately provide an anatomic analog of recruitment that reflects changes in tissue density and has the potential to reveal the regional responses of ventilation and aeration.

It must be emphasized that recruitment maneuvers are of unproven safety and do not always improve oxygenation. The best technique with which to perform a recruitment maneuver is currently unknown and may well vary with circumstances. In some instances, using high levels of pressure to control ventilation for several minutes may be preferable when compared with an equally high level of pressure sustained for 40 seconds or vice versa. As already noted, it appears that the contour of the inspiratory pressure volume curve of the respiratory system may be used to reflect the relationship between recruitment and airway pressure. In its upper inflection zone, therefore, the curve may give some guidance related to the level of pressure necessary to achieve near-maximal lung opening. Once the lung is opened to the maximal extent possible, applied pressure should be released in stages using oxygenation and perhaps inspiratory deflation mechanics to identify the appropriate PEEP level that sustains full recruitment. Gas exchange measurements may also help to signal when recruitment maneuvers should be attempted again.

**Is PEEP Itself a Recruitment Tool?**

A widely recognized approach to ventilation in acute lung injury that incorporates a low tidal volume strategy for mechanical ventilation includes sufficient PEEP to maintain maintenance of an “open lung.” Here, emphasis is placed on establishing and maintaining patency of all potentially recruitable airspaces throughout the tidal cycle. The primary motivation is lung protection; although high tidal pressures are an independent contributor to lung injury, the effects of high tidal pressures are dramatically attenuated by using sufficient PEEP, suggesting that serious damage may occur when collapsed units reopen repeatedly under high tidal pressure. As already noted, stresses at the junctions of closed and open airspaces spaces rise considerably above those in patent units, generating forces and dissipating energy in the expanding tissues proportionate to applied transpulmonary pressure. Epithelial injury has been attributed to this process.

Unless the lung is fully open—or successfully resists opening—recruitment may extend over the entire total lung capacity range. By implication, some lung units may be repetitively exposed to high levels of stress arising from collapse and reopening during the tidal cycle. Although “sticky” lung units may occur elsewhere in the lung, this dynamic stress may predominate in midzone and dependent lung regions that are compressed by the superimposed pressure of the overlying lung they support and are subject to absorption at atelectasis. Because PEEP counterbalances the increased tendency for closure and small tidal volumes limit peak tidal pressure, a high PEEP–low tidal volume strategy may offer the best chance of avoiding injurious cycles of closure with reopening that occur at high inspiratory pressure.

**Why Not Just Use High PEEP?**

High levels of PEEP have potential drawbacks. Apart from their adverse hemodynamic impact, PEEP-driven increases of peak, mean, and end-expiratory alveolar pressures tend to redirect blood flow through less compliant, less well-aerated areas, increasing ventilatory dead space. Occasionally, PEEP impairs rather than improves oxygen transport. Overexpansion of lung units that are already patent increases the tractive forces applied to their associated vasculature, accentuates junctional stresses at the interface of open units and adjacent units that remain closed, and may actually compress nearby ventilated airspaces that are less compliant (Gattinoni L, Amato M, personal communication). These are important considerations because at most inflation pressures, recruitable, consolidated, and fully open lung units coexist in the acutely injured lung.

In formulating an “open lung” strategy, it must be understood that PEEP holds open unstable lung units but, as a rule, does little to open them itself when peak inspiratory alveolar pressure remains unchanged. Sustained high pressures are required to open these unstable lung units. Although maximal distension is normally attained within a healthy lung by an alveolar to pleural pressure difference of approximately 30 cm of water, pressures more than twice as great may be needed to open some refractory, but potentially recruitable, lung units. Recruitment maneuvers are intended to establish
initial alveolar patency that can then be maintained at lower tidal pressures and PEEP levels than would otherwise be required. In the injured lung, surface tension and adhesive forces must be overcome during inspiration that are not in play during expiration.

Both adequate pressure and time are clearly important to the recruitment process, but for a specified PEEP and tidal volume combination, other factors influence whether patency is established or maintained. As already mentioned, spontaneous breathing effort helps to distribute tidal volume to the dependent, peridiaphragmatic zones most susceptible to atelectasis. However, forceful expiratory efforts might also promote the collapse-reopening cycle. The pattern with which a given average tidal volume is applied may also contribute: after gas reabsorption, opening of some lung units does not occur smoothly and homogenously but in a series of “pops,” a discontinuous propagating cascade or avalanche of aeration. This inconsistent pattern of lung unit opening and closure may explain why “biologically variable” ventilation maintains gas exchange better than a monotonous pattern of unchanging tidal volume for an equivalent minute ventilation. Prone positioning is another attractive means toward recruiting in that it applies and sustains high tractive forces in the dorsal regions that are compressed in the supine position by the weight of the heart and mediastinal contents. Other methods to improve either distribution of opening forces or relative recruitability of those areas more difficult to expand (such as modification of regional chest wall compliance) hold promise for the future.

Epilogue: Where Are We Now?

Given these principles of raising pressure, extending time, and varying breathing pattern, diverse methods have been suggested to help accomplish recruitment without applying high tidal cycling forces. How best to perform episodic recruitment maneuvers, however, has not been determined and may well vary with underlying pathophysiology. Intermittent sighs, episodic increases of PEEP, stepped increases of PEEP with a capped peak inflation pressure, and sustained application of a pressure that achieves or exceeds total lung capacity have all been proposed and tested (Table 1). Although each type of maneuver may succeed to some extent, the maneuvers are not necessarily equally effective or equally safe in any given patient. Sustained high pressure may cause transient hemodynamic compromise, expose the fragile lung to barotrauma, and, when repeated frequently, inflict injury that is not apparent after isolated procedures. When successful, the benefits of recruitment maneuvers tend to fade over time, unless sufficient end-expiratory pressure is sustained by PEEP or other maneuvers such as prone positioning. Maximizing deflationary tidal compliance after a recruitment maneuver has been proposed to identify the ideal PEEP value, but, though plausible, the effectiveness and generalizability of this mathematics-based theoretical argument have not yet been confirmed clinically.

There are other fundamental questions to be answered. Should recruitment be our objective when opening closed lung regions requires such high pressures that tidal opening and closure would not otherwise occur? Does aeration help the inflamed lung to heal or should such tissues be allowed to rest? What is the most effective recruitment method? How should recruitment be monitored: by mechanics, gas exchange, or both? Are serial recruitment maneuvers needed in clinical practice, and if so, how closely should they be spaced? Perhaps, as we have previously suggested, recruitment like other ventilator strategies must be adapted to specific patient pathology. Convincing answers to these and other questions will require careful laboratory and bedside observation.

### TABLE 1. Recruitment Maneuvers*

<table>
<thead>
<tr>
<th>Technique</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>High PEEP/CPAP</td>
<td>40–60 cm H₂O for 30–90 seconds (no machine breaths)</td>
</tr>
<tr>
<td>High PEEP/CPAP with PCV</td>
<td>PEEP to 20–40 cm H₂O together with PCV 10–20 cm H₂O</td>
</tr>
<tr>
<td>Frequent intermittent sighs</td>
<td>PEEP elevation for 2 consecutive breaths twice each minute</td>
</tr>
<tr>
<td>Extended sigh (or stepped PEEP)</td>
<td>Stepped increase in PEEP to 15, 20, 25 and 30 cm H₂O with decline in steps after highest level of PEEP. Each step 30 seconds. All steps included machine breaths except highest PEEP Level.†</td>
</tr>
<tr>
<td>Increased PEEP with preserved inspiration pressure</td>
<td>Stepped increase in PEEP with maintenance of previous tidal volume over 30 seconds to 2 minutes</td>
</tr>
<tr>
<td>Increased PEEP with limited peak inspiratory pressures</td>
<td>Stepped increases of PEEP with limitation of peak inspiratory pressure</td>
</tr>
</tbody>
</table>

*Risks include overt barotrauma, volutrauma, hypoxemia, and hypoventilation. To date no technique has been demonstrated superior.


### REFERENCES

4. Brower RG, Shanhillt CB, Fessler HE, et al. Prospective, randomized, controlled clinical trial comparing traditional versus reduced tidal vol-
32. Hickling KG. Best compliance during a decremental, but not increment- al, positive end expiratory pressure trial is related to open-lung positive end expiratory pressure. *Am J Respir Crit Care Med*. 2001;163:69–78.